NOVEL METHODS OF DIRECTED EVOLUTION

ABSTRACT OF THE DISCLOSURE

5   Methods for generating chimeric polynucleotides by directed evolution are described. In the methods, splice points of interest are identified within the polynucleotides of a basis set of polynucleotides, preferably through the use of an algorithm that defines the number of splice points and selects the splice points, either by random selection or using information regarding alignment of the polynucleotides. The

10   algorithms can include additional factors, including a definition of a desired distance between splice points, and/or weighing factors to bias selection of splice points. Chimeric polynucleotides are generated using primers (e.g., double primers or non-overlapping primers) and polymerase chain reaction or combinatorial strategies.